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Filed: September 9, 2003
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Attorney Docket No.: CIT1620-1

REMARKS

Claims 2, 15, 26, and 42 have been canceled without prejudice or disclaimer. Claims 1, 8, 11, 14, 16-18, 23-25, 32, 35, and 38-41 have been amended. New claims 43-46 have been added. Subsequent to the entry of the present amendment, claims 1, 3-14, 16-25, 27-41, and 43-46 are pending and at issue. These amendments and additions add no new matter as the claim language is fully supported by the specification and original claims.

I. Amendment to the Specification and Claims

Claims 1, 14, 16 and 17 have been amended to clarify that the non-human animal is a mouse. Support for the amendments can be found throughout the specification and claims, particularly in claim 15 as filed. Accordingly, the amendments to claims 1, 14, 16 and 17 add no new matter.

Claims 1, 8, 11, 14, 16-18, 23-25, 32, 35, and 38-41 have also been amended to correct errors of a typographical and technical nature. As such, these amendments add no new matter.

New claims 43-46 have been added. Support for new claims 43 and 44 can be found, throughout the specification and claims as filed, *e.g.* at pages 2-4, 8, 10-11, 15-16, 24-26 and 29-31. Support for new claims 45-46 can be found particularly in claim 1, as filed. Accordingly, no new matter has been added by way of these additions and no new search is required..

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II. Absence of Prior Art Disclosure of Claims 1-40

The Office Action states that “[t]he subject matter of claims 1-40 are free of the prior art of record, which does not disclose or fairly suggest the DNA constructs required by the instant claims.”

III. Information Disclosure Statement

According to the Examiner, the Information Disclosure Statement filed May 6, 2004 “fails to fully comply with 37 CFR 1.98(a)(2)” because “[o]nly the first page (cover sheet) [of PCT Application No. WO 01/11951] was provided.” Office Action at p. 2.

Applicants remind the Examiner that only material information is required to be disclosed and that materiality is defined under the Patent Rules to exclude information that is “cumulative of information already of record or being made of record in the application.” *See* 37 C.F.R. §1.56(b). The Information Disclosure Statement filed on May 6, 2004 disclosed items cited in a communication from a foreign patent office in a counterpart application. In the foreign communication, both PCT Application WO 01/11951 and European Patent Application EP1 206 906 A1 were cited. EP1 206 906 A1 is the European counterpart of WO 01/11951, as noted on the Form PTO 1449 and as such has a disclosure which is substantially identical to WO 01/1195. Since the European equivalent of WO 01/1195 was provided, it is not necessary for Applicants to provide a copy or even to disclose the PCT document as it is merely cumulative of art being made of record in the application. Applicants submit that the PCT application was listed for the convenience of the Examiner, so that he would be alerted to the citation by the foreign patent

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office and so that he would recognize the document as the equivalent of properly disclosed EP1 206 906 A1, in the event that the PCT application turns up in the Examiner's a search.

Accordingly, Applicants submit that the Information Disclosure Statement filed May 6, 2004 fully complies with 37 C.F.R. §1.98(a)(2) and an acknowledgment to that effect respectfully requested.

IV. **Objections to the Claims**

Claims 18 and 25-40 have been objected to for allegedly containing informalities, as listed below. Office Action at p. 2.

Claim 18. According to the Examiner, the recitation of "a first and second non-human animal DNA sequences" (line 5) is grammatically improper, and "the human DNA" should be — the human DNA coding sequence." *Id.*

Claim 18 has been amended to improve the grammar and as suggested by the Examiner, to clarify that "the human DNA" is "the human DNA coding sequence."

Accordingly, withdrawal of the objection to claim 18 is respectfully requested.

Claims 25-40. According to the Examiner, the "process steps of claim 25 go beyond a method of making a DNA construct" as recited in the preamble, and are therefore improper. Office Action at p. 2. According to the Examiner, claim 26 "adds steps that go even farther beyond the making of a DNA construct, where the ES cell is implanted in a pseudopregnant non-human animal." *Id.*

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Claim 25 has been amended to delete the step of "introducing the recombinant DNA construct into a non-human embryogenic stem cell." Claim 26 has been cancelled. Applicants submit that the process steps of claim 25, as amended, are consistent with the preamble to that claims.

Accordingly, withdrawal of the objection to claims 25 -40 is respectfully requested.

V. Rejections under 35 U.S.C. §112, First Paragraph

Claims 1-17 and 25-41 have been rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enablement. Office Action at p. 3. The Examiner states that "the specification, while being enabling for embodiments wherein the non-human animal is a mouse, the non-human animal DNA of the first construct is a mouse genomic DNA comprising mouse DNA that is homologous to the human DNA sequence that is immediately flanked by first and second mouse sequences that are homologous to the flanking first and second mouse genomic DNA sequences that flank the human DNA sequence in the second construct, the embryogenic stem (ES) cell is a mouse ES cell, the non-human blastocyst is a mouse blastocyst, and the pseudopregnant non-human animal is a pseudopregnant mouse, does not reasonably provide enablement for any other embodiments embraced by the claims." *Id.*

Independent claim 1 and dependent claims 14, 16 and 17 have been amended to recite that the non-human animal is a mouse. Claims 2 and 15 have been cancelled. Applicants submit that claims 1-17, as amended, encompass embodiments of the invention that the Examiner found to be enabled.

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Independent claim 25 has been amended to omit the phrase “introducing the recombined third DNA construct into a non-human embryonic stem cell.” Applicants submit that homologous recombination within cells other than mouse ES cells was well known in the art at the time of the invention and therefore, independent claim 25 and claims 26-40, which depend from claim 25, are enabled by the specification when considered in light of the knowledge of skilled artisan at the time the invention was made.

Accordingly, reconsideration and withdrawal of the rejection of claims 1-17 and 25-41 under 35 U.S.C. § 112, first paragraph is respectfully requested.

VI. Rejections under 35 U.S.C. § 112, Second Paragraph

Alleged Omission of Essential Steps

Claims 1-17 have been rejected under 35 U.S.C. §112, second paragraph, as being “incomplete for omitting essential steps, such omission amounting to a gap between the steps.” Office Action at 7. According to the Examiner, “[t]he omitted steps are introducing the embryogenic stem cells into a non-human blastocyst and implanting the chimeric blastocyst into a pseudopregnant non-human animal, which then carries to term a humanized animal arising from the implanted blastocyst.”

Solely for the purposes of advancing prosecution, Claim 1 has been amended as suggested by the Examiner. Applicants submit that the rejection of claims 1-17 is moot in view of the amendments to the claims.

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Accordingly, reconsideration and withdrawal of the rejection of claims 1-17 under 35 U.S.C. § 112, second paragraph is respectfully requested.

Alleged Indefiniteness

Claims 2, 8, 11, 15-24, 26, 32, 35, and 38-40 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite, as detailed below. *See* Office Action at 7.

The Examiner alleges that various claims provide “insufficient antecedent basis” for the following terms:

1. In claims 2 and 26 “the embryogenic stem cells.”

Claims 2 and 26 have been cancelled for unrelated reasons. Applicants submit that rejection of claims 2 and 26 is moot in view of the cancellation of these claims.

Accordingly, reconsideration and withdrawal of the rejection of claims 2 and 26 under 35 U.S.C. § 112, second paragraph is respectfully requested.

2. In claims 8 and 32 “the human gene sequence.”

Claims 1 and 25, from which claims 8 and 32 depend, respectively, have been amended to recite a single occurrence of “a human DNA sequence” and claims 8 and 32 have been amended to recite “the human DNA sequence.” Applicants submit that the rejection of claims 8 and 32 is moot in view of the amendments to the claims.

Accordingly, reconsideration and withdrawal of the rejection of claims 8 and 32 under 35 U.S.C. § 112, second paragraph is respectfully requested.

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3. In claims 11 and 35, "the intron."

Claims 11 and 35 have been amended to recite "the at least one intron." Applicants submit that the rejection of claims 11 and 35 is moot in view of the amendments to the claims as the limitation "at least one intron" is found in the claims from which claim 11 and 35 depend.

Accordingly, reconsideration and withdrawal of the rejection of claims 11 and 35 under 35 U.S.C. § 112, second paragraph is respectfully requested.

4. In claims 14 and 38, "the non-human animal DNA sequence."

Claims 14 and 38 have been amended to recite "the first or the second ... DNA sequence." Applicants submit that the rejection of claims 14 and 38 is moot in view of the amendments to the claims.

Accordingly, reconsideration and withdrawal of the rejection of claims 14 and 38 under 35 U.S.C. § 112, second paragraph is respectfully requested.

5. In Claim 15, "the non-human animal" and "the non-human embryonic stem cells."

Claim 15 has been cancelled. Applicants submit that the rejection of claim 15 is moot in view of the cancellation of this claim.

Accordingly, reconsideration and withdrawal of the rejection of claim 15 under 35 U.S.C. § 112, second paragraph is respectfully requested.

6. In Claim 18, lines 6-7, "the non-human animal."

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Claim 18 has been amended to recite "a first non-human animal DNA sequence and a second non-human animal DNA sequence" at lines 5-6, thereby providing the antecedent basis for the limitation of "the first and second non-human animal DNA sequences" at line 7, as amended. Applicants submit that the rejection of claim 18 is moot in view of the amendments to the claims.

Accordingly, reconsideration and withdrawal of the rejection of claim 18 under 35 U.S.C. § 112, second paragraph is respectfully requested.

7. In claim 23, "the start codon."

Claim 23 has been amended to recite "wherein the human DNA coding sequence comprises a start codon" prior to the recitation of "the start codon." Applicants submit that the rejection of claim 23 is moot in view of the amendments to the claims.

Accordingly, reconsideration and withdrawal of the rejection of claim 23 under 35 U.S.C. § 112, second paragraph is respectfully requested.

8. In claim 24, "the stop codon."

Claim 24 has been amended to recite "wherein the human DNA coding sequence comprises a stop codon" prior to the recitation of "the start stop." Applicants submit that the rejection of claim 23 is moot in view of the amendments to the claims.

Accordingly, reconsideration and withdrawal of the rejection of claim 24 under 35 U.S.C. § 112, second paragraph is respectfully requested

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The Examiner also states that claims 8 and 32 recite the limitation “sequence is ... genes,” and alleges that “it is unclear if the sequence can comprise a gene or must comprise multiple genes.” Office Action at p. 8. The Examiner also states that “the list that follows ‘genes encoding’ is a list of proteins and genes. Genes do not encode genes. Also, it is unclear what ‘insulin receptors immunoglobulins metabolic pathway genes refers to,” and suggests language for the claim. *Id.*

Claims 8 and 32 have been amended as suggested by the Examiner. Applicants submit that the rejection of claims 8 and 32 is moot in view of the amendments to the claims.

Accordingly, reconsideration and withdrawal of the rejection of claims 8 and 32 under 35 U.S.C. § 112, second paragraph is respectfully requested.

The Examiner also states that “claims 16, 17, 39, and 40 are allegedly “unclear with respect to how the human DNA sequence and the non-human DNA sequence ‘are joined to’ the start or stop codons, and whether the start or stop codons are part of the human DNA sequence or not.” It is presumed that the human DNA sequence comprises the start or stop codon at its 5' or 3' end, respectively, to which the first or second non-human animal DNA sequence, respectively, is joined, but that is not what the claims recite.

Claims 16 and 39 have been amended to clarify that the human DNA coding sequence comprises a start codon having a 5' end and to which the first mouse or non-human DNA sequence, respectively, is joined. Claim 17 and 40 have been amended to clarify that the human DNA coding sequence comprises a stop codon having a 3' end to which the second mouse or non-human DNA

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sequence, respectively, is joined. Applicants submit that rejection of claims 16, 17, 39 and 40 is moot in view of the amendments to the claims.

Accordingly, reconsideration and withdrawal of the rejection of claims 16, 17, 39 and 40 under 35 U.S.C. § 112, second paragraph is respectfully requested

VII. Rejection under 35 U.S.C. § 102

Claims 41 and 42 have rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Stacey *et al.*, *Mol. Cell. Biol.* 14: 1009-1016, 1994. According to the Examiner, "Stacey et al. describes a humanized mouse comprising a human α -lactalbumin gene in place of the endogenous mouse α -lactalbumin gene. The targeting vector used to make the mouse was made by a different method than the third DNA construct recited in instant claim 1. However, an analogous mouse made by the method of instant claim 1 would produce a mouse with the same humanized α -lactalbumin gene." Office Action at 9-10

In order for a reference to anticipate, the reference must teach each and every element of the claim. *See* MPEP 2131.

Claim 41 has been amended to recite that the human DNA is selected from a G-protein coupled receptor gene, a kinase gene, a phosphatase gene, an ion channel gene, a nuclear receptor gene, an oncogene gene, a cancer suppressor gene gene, a viral receptor gene, a bacterial receptor gene, a P450 gene gene, an insulin receptor gene, an immunoglobulin gene, a metabolic pathway gene, a transcription factor gene, a hormone receptor gene, a cytokine gene, a cell signaling pathway gene and a cell cycle gene. Claim 42 has been cancelled. As

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acknowledged by the Examiner, Stacey *et al.*, teaches α -lactalbumin, which is not one of the enumerated DNA sequences of claim 41. As such, Stacey *et al.* does not teach each and every limitation of claim 41, and therefore does not anticipate claim 41.

Accordingly, withdrawal of rejection of claims 41 and 42 under 35 U.S.C. §102 (b) is respectfully requested.

VIII. Double Patenting

The Office Action states that “should claims 1-14,16, and 17 be found allowable, claims 25-40, respectively, will be objected to under 37 C.F.R. §1.75 as being a substantial duplicate thereof.” Office Action at p. 10.

Claim 25 has been amended to omit the final process step. Claims 25-40 are now clearly directed to making a construct, not a mouse. Therefore, claims 25-40, as amended, are not a substantial duplicate of claims 1-14, 16 and 17. Acknowledgment to this effect is respectfully requested.

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CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if it is believed that prosecution can be assisted thereby.

No fee is deemed necessary with the filing of this paper. However if any fees are due, the Commissioner is hereby authorized to charge any fees, or make any credits, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal Sheet is enclosed.

Respectfully submitted,



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